REMARKS/ARGUMENTS

These remarks are filed in response to the Examiner's Report of March 16, 2009, a response to which is due by June 16, 2009. Since the Examiner's Report was FINAL, these remarks are filed in conjunction with a Request for Continued Examination. Our deposit Account No. 13-2400 is being charged in the amount of $405 to cover the required Request for Continued Examination fee for a small entity.

Claims 37-39 and 41-43 stand. Subject matter from claim 48 has been incorporated into claims 37 and 39. No new matter has been added by the present claim amendments.

Claim Objections

The Examiner has objected to claim 48 for an informality related to antecedency. Applicant has cancelled claim 48, rendering the Examiner's objection moot.

35 USC 103

The Examiner has rejected claims 29-39, 41-46 and 48 under 35 USC 103(a) as being unpatentable over Mezei et al. (U.S. Patent No. 5,451,408) or Mezel et al. (RE 38,407) in view of Dershwitz et al. ("Pharmacokinetics and pharmacodynamics of inhaled versus intravenous morphine in healthy volunteers," Anethesiology, 2000, 93(3), pp. 619-628 (Abstract Only)) and Shafer et al. ("Pharmacokinetics, Pharmacodynamics, and Rational Opioid Selection,", Anesthesiology, 1991, 74(1), pp. 53-63 (Abstract Only)). Applicant has cancelled claims 29-36, 44-46 and 48, rendering this rejection with regards to those claims moot.

The Examiner confirms that Mezei/Mezel lacks the express teaching of (1) continuous inhalation via a pulmonary drug delivery device, (2) administration is

solely through the conscious effort of the user, (3) device mass of 250-2,500 gm (4) an outlet in the device through which the formulation is dispensed and (5) the intended pharmacokinetic profile of the claimed formulation upon administration. The Examiner states that these deficiencies are obvious per the teachings of Mezei/Mezel and/or are obviated by the teachings of Dershwitz and Shafer.

Notably, the Examiner has stated that an ordinary skilled artisan would have had a reasonable expectation of success in continuously administering the Mezei/Mezel formulations until sufficient analgesia was obtained. Regarding the relative amount of the two opioids, the amount of a specific ingredient in a composition is clearly a result effective parameter that a person of ordinary skill in the art would routinely optimize. Optimization of parameters is a routine practice that would be obvious for a person of ordinary skill in the art, and it would have been customary for an artisan of ordinary skill to determine the optimal amount of each ingredient to achieve the desired results. Thus, absent some demonstration of unexpected results from the claimed parameters, the optimization of ingredient amoutns would have been obvious at the time of applicant's invention.

Applicant respectfully traverses, with a special emphasis on the fifth of these factors, namely that the intended pharmacokinetic profile of the claimed formulation would be obvious per the teachings of Mezei/Mezel and/or obviated by the teachings of Dershwitz and Shafer, especially when this fifth teaching is combined with the second teaching – that of administration solely through the conscious effort of the user. Further, Applicant agrees that, the amount of a specific ingredient in a composition is a result-effective parameter that a person of ordinary skill in the art would routinely optimize, and that optimization of parameters is a routine practice and that is customary for a person of ordinary skill to determine the optimal amount of each ingredient to achieve the desired results. However, to optimize ingredients in a formulation, one must have a specific objective in hand; that objective has consistently been taught in the prior art to be the formation of an extended release formulation. In Mezei/Mezel, the formulation

was optimized; an optimal formulation of 10-20% free fentanyl and 80-90% liposomally encapsulated fentanyl (w/w as a percentage of active drug) was taught. This was an optimized formulation, for the purpose of providing adequate rapid onset of opioid action, followed by an effect that was as sustained as possible.

The surprising and unexpected result from the claimed parameters, specifically, the intended pharmacokinetic profile (driven by the ratio of fentanyl to liposomally encapsulated fentanyl in the formulation), and administration through the conscious effort of the patient (two parameters the Examiner confirms are novel) is that the effects of mild ventilatory depression and fatigue occur well before the more toxic effects of the drug, in a manner that a patient can identify. Thus, the admittedly novel and claimed parameters result in the unexpected result that a patient can self-administer the opioid formulation, titrating the dosage "to effect", and knowing when to stop administration.

This unexpected result could not be achieved through "routine experimentation" because all of the prior art, as cited by the Examiner, taught a completely different "routine optimization" process, for a completely different desired result. A person of ordinary skill in the art can only routinely optimize parameters, without an inventive step, if they know the result they are optimizing for. A person of ordinary skill in the art, routinely optimizing parameters using the teachings of the prior art for guidance, would be optimizing the parameters to create a longer lasting drug, which is all the prior art taught as desired. Though Stanley (US Patent No. 5,288,498) purportedly teaches dose-to-effect dosing of opiates by patients, this involves an elaborate drug containment matrix, and an mucosally-administered drug. A person of ordinary skill in the art, routinely optimizing parameters using the teachings of the prior art for guidance, would not, without an inventive step, apply Stanley to an inhaled, liposomally encapsulated fentanyl product and attempt to create a dose-to-effect formulation. In fact, Stanley teaches against the present invention, since it creates an overly elaborate system to achieve the same effect – an effect that would have been much more elegantly and easily achieved by the

present invention, had it been obvious to do so.

One of the key distinctions between the present invention and the prior art is that, in the prior art, patients are medicated by attending professionals. For example, in Mezei, as well as Dershwitz and Shafer, it was specifically taught, or would be inferred by a person skilled in the art, that a professional would decide on the dosing amount and would medicate the patient. This professional involvement requires time, energy and judgement calls on the part of the professional when determining how much medication to dispense, since an individual's perception of pain, and an individual's reaction to opioids for the mitigation of said pain, vary radically from one person to another. In the present invention, the medication process is controlled solely by the pain sufferer. In the prior art, the risk to a self medicating pain sufferer is, of course, that pain relief might be experienced only after the patient has dosed themselves to opioid levels that are toxic, given the delay in the onset of opioid effects. This is addressed in the present invention by providing a composition that allows the patient to experience pain relief during a dosing session. That dosing session can then be stopped by the user before ingesting toxic amounts of the opioid.

The invention is unique and unobvious in providing a system by which the end-user can be responsible for medicating themselves to reduce pain using opioids that risk significant toxicity upon overdose. The present system takes drug and dosing into consideration to allow end-users to experience pain relief and/or side effects that are the patient's key to stop dosing and avoid toxicity.

Moreover, the present invention contemplates a method that allows and enables the pain sufferer and user to take responsibility for dosing, with attendant risk of overdose. This overdose risk is mitigated when the method is applied using the present opioid composition and delivery system. Other approaches, including all of the approaches cited by the Examiner, use either professional managed care or instrumentation to intervene or control the user's intake of the medicine when a

pulmonary delivery system is used.

In order to clarify the ambit of protection sought, applicant has amended claim 12 to add the limitations of claims 18 and 56. Applicant has also amended claims 28 and 29 to add the limitations of claims 37 and 56. To further clarify the ambit of protection sought, the Applicant has removed all claims to opioid formulations other than opioid formulations comprising fentanyl and liposomally encapsulated fentanyl. Applicant has not done this in response to any specific objections of the Examiner, but, rather, to better claim the desired commercial embodiment and to focus and clarify the ambit of protection sought.

Double Patenting

The Examiner has rejected claims 37-39, 41-45 and 48 on the ground of non-statutory obviousness-type double patenting as being unpatentable over claims 1 and 10-25 of U.S. Patent No. RE 38,407 in view of Dershwitz et al. Applicant respectfully submits that the reasons for this double patenting rejection are identical to the reasons provided for the Examiner's 35 USC 103 rejection of these same claims. As such, applicant respectfully submits that the amendments and arguments presented above with respect to obviousness also address the Examiner's rejections with respect to double patenting.

Conclusion

It is respectfully submitted that the present amendments and remarks herein are a complete response to all outstanding issues. Favourable consideration is respectfully requested. If the Examiner believes a telephone conference would advance the prosecution of this application, the Examiner is invited to telephone the undersigned at the below-listed telephone number.

Respectfully Submitted,
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